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PROPHYLACTIC INOCULATIONS AGAINST INFECTIOUS DISEASES

- USSR -

by A.F. Blyuger

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## PROPHYLACTIC INOCULATIONS AGAINST INFECTIOUS DISEASES

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## VANISHED DISEASES

The constant increase in the material and cultural level of the Soviet people, the government system of health protection, and the great achievements of this country's medical science create all the conditions for the complete elimination of some infectious diseases in our country and for a marked reduction in the morbidity of others.

Soviet medical science has achieved great successes in the most varied fields: in the use of atomic energy in the treatment of a number of diseases; devising of major operations on the lungs, heart, and blood vessels; treatment of many diseases with blood transfusions and all possible blood preparations; creation of powerful antibiotics, chemotherapy preparation, and other highly effective drugs. However, the greatest and most graphic successes are those achieved in the control of many infectious diseases.

For hundreds of years mankind has suffered from smallpox, cholera, and plague which have taken a vast number of human lives. In the 18th Century more than 400,000 people fell victim annually to smallpox in Western Europe, and many thousands remained invalids. In those times two-thirds of all people born were affected with small-pox. Epidemics (mass affections) of Asiatic cholera spread over the world six times, striking millions of people. In prerevolutionary Russia alone more than 2 million people perished during an epidemic of cholera.

The so-called Justinian plague, a world epidemic that broke out in the Byzantine Empire in the 6th Century, lasted for 50 years and brought death to over 100 million people. A quarter of the European population fell victim to a second epidemic of the plague in the 14th Century. In view of these terrible figures it becomes clear how outstanding is the achievement of Soviet health protection of eliminating completely all the so-called especially dangerous infectious diseases from the territory of the USSR.

The final victory over cholera was attained by doctors in 1926 and from that time not a single case of this disease was recorded in our country. In 1936 the last isolated case of smallpox diseases disappeared in the USSR, and plague affliction, the foci of which had previously existed on considerable territory of the southeastern regions of the European part of our country, was wiped out.

Not only have the "especially dangerous" infectious diseases become a thing of the past, but the list of vanished diseases is being constantly augmented. Placed in this category is recurrent fever, a serious debilitating disease, epidemics of which never ceased in the worker's districts and rural areas of tsarist Russia. Suffering the same fate was filiariasis Medinensis, a serious disease affecting some areas of Central Asia and caused by a special worm penetrating under the skin and causing painful swellings and poorly healing ulcers.

To eliminate these diseases was not an easy task. The road that led to their elimination was long and difficult. The history of the study and control of these diseases is full of examples of great heroism of the doctors, brave conjectures and painstaking work of many researchers. The Russian physicians gave all their energy and some even their lives in the control of these terrible diseases. Here is one example of such a hero: Dr. I. A. Deminskiy, who became infected with plague in 1912 during scientific experiments, sent his colleagues a telegram containing the following: "Have become infected with pulmonary plague. Take available cultures. 1. Perform an autopsy on my body as on a case of experimental infection from a ground-hog". Our country's science knows many such examples of noble service to science, examples of self-denying work associated with danger to the life of the researcher for the benefit of mankind.

Then what influences the spread of epidemics, and by what means was the elimination of many mass diseases achieved?

The most important factors influencing the spread of infectious diseases are living conditions, conditions of alimentation, type of work and also the level of the sanitary culture of the population. Harsh living conditions of a people, low sanitary culture, cruel exploitation of the working class are the main reasons for the fact that many infectious diseases including smallpox, and plague that had long ago been eliminated in our country are still prevalent in some capitalist and especially in colonial countries. For example, in 1945, a total of 53,737 people became ill with plague throughout the world; cases of this disease were observed in France, Spain, Italy, Portugal and other European countries. Many thousands of people in the British colonies still become sick with smallpox and cholera. There have been outbreaks of smallpox up to very recent times even in Britain itself.

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1. Microbes grown in the laboratory.



Under the conditions of the Soviet socialist government a colossal increase in the economic well-being and sanitary culture of the population have become the deciding factors which have brought about the achievement attained in the control of many infectious diseases. Medical personnel of all specialities and primarily the regional physicians are engaged in the prevention and control of infectious diseases in our country. The leadership of this work is concentrated in the hands of a special organization -- The Sanitary-Anti-epidemic Service. The basic organization of this service in local areas is the sanitary-epidemiological station. Should an infectious disease appear in any corner of our great Fatherland, the regional physician immediately notifies the sanitary-epidemiological station. Physicians -- epidemiologists are immediately dispatched from the station to patient. Their assignment is to prevent the spread of the disease, to stifle the epidemic at its source.

Epidemiology -- the science concerning the laws governing the spread of infectious diseases and the organization of their control, knows of many ways not only to check the outbreak of infectious diseases, but also to prevent their occurrence. Disease prevention is the basic objective facing the Soviet department of health.

An important role in preventing infectious diseases belongs to prophylactic inoculations. These inoculations immunizing the human organism to some infectious diseases are a distinguished achievement of medical science. Twenty years ago they made possible the complete elimination of smallpox in our country; at the present time they make it possible to aim towards the complete elimination of some other infectious disease, primarily, of diphtheria.

To understand how physicians achieve artificial immunity to various diseases, it is necessary to learn how the human body fights against microbes,<sup>2</sup> the causative agents of these diseases under natural conditions, and what defense mechanisms it possesses.

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2. A microbe is a minute, live organism which can be seen only under a microscope. A number of microbes cause infectious diseases (diphtheria, poliomyelitis, etc) when they enter the human body.

## IMMUNITY TO INFECTIOUS DISEASES

Disease-producing microbes that have penetrated into the human body encounter obstacles to their development and vital functions from the very moment of their contact with the skin and mucous membranes. The skin is a reliable barrier against most of the disease-producing microbes; it not only presents a mechanical obstacle to the penetration of the microbe into the body, but also excretes special substances having a fatal effect upon the microbes, the causative agents of many infectious diseases. It is very important to mention that these microbicidal substances are excreted only by a clean skin. Thus, the microbes of typhoid fever perish very quickly on a well washed skin, but are able to survive for a long time on a dirty skin.

The mucous membranes covering the oral and nasal cavities as well as the eyes, genital organs, and the respiratory tract are an equally reliable defense of the organism against microbes. The mucous membranes also excrete special substances, deadly for the microbes. Some of these substances are well known. For example, the native scientist P.I. Lashchenkov has isolated from the lacrimal fluid that irrigates the eye a special substance -- lysozyme. Lysozyme is contained also in saliva, breast milk, intestinal juice and some tissues. It is due to the presence of lysozyme that there are no microbes on the mucous membranes of the eyes although microorganisms constantly get into the eye in air and dust. In the oral cavity, scratches and injuries heal rapidly owing to the presence of bactericidal substances.

The gastric and intestinal juice and bile also form a kind of "barrier" for many microbes. In many cases microbes penetrating into the organism, as for instance the microbes of dysentery and typhoid, perish in the stomach under the action of the gastric juice before they can multiply and cause disease.

The statements of Soviet researchers on the defensive role of some microbes harmless to man that are constantly present in the oral and nasal cavities as well as in the intestinal tract and the vagina of healthy people are of special interest. L.G. Perets has established that many of these microbes produce substances hindering the development of, and having a destructive influence on disease producing microbes.

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### 3. bactericidal substances -- substances that kill bacteria.

As a result of the vital activity of intestinal microbes habitually present in healthy organisms, conditions are established under which causative agents of infectious diseases are quick to disappear.

Should the disease-producing microbes break through the defensive barrier formed by the skin and mucous membrane and the action of saprophytes, and penetrate into the tissues of the organism, new obstacles appear in their way in the form of the lymphatic system consisting of the vessels and nodes through which flows a clear liquid called lymph that irrigates all the organs and tissues of the body. The lymphatic nodes are located in all organs and tissues: under the skin, in the pharynx (pharyngeal and palatine tonsils at the base of the tongue), in the intestines, stomach, etc. They consist of connective tissues forming a network of sinuses. Their structure is reminiscent of the structure of a sponge that consists of cells in groups of various sizes. These cells are able to catch microbes.

Before entering the blood the microbes pass through the lymphatic nodes where they are stopped and then seized by the cells. Not only live microbes, but also particles of dust (for instance in the nodes surrounding the respiratory tract), dyes (for instance in tattooed people) and also various chemical substances are caught in the nodes. In stopping the microbes the lymphatic nodes may become inflamed and enlarged. Their inflammatory process limits the spread of microbes through the body.

Only if the microbes break through the lymphatic barrier do they penetrate into the blood. Should this happen, the organism would still not be left defenseless against the microbes, as the blood itself possesses marked defensive properties. Scientists noticed long ago that if disease producing microbes were put into a test-tube containing blood, they quickly perished. Later, it became possible to establish that this property of the blood depended on the presence in it of a special defensive substance called the complement or alexin (from the Greek word -- "alexo -- I defend"). The complement is able to act against various microbes causing their destruction.

A special role in defending the organism against microbes belongs to the white blood cells -- the leucocytes. The importance of these cells in controlling microbes was determined by the prominent Russian scientist I.I. Mechnikov. I.I. Mechnikov showed in his experiments that if the spores<sup>4</sup>

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<sup>4</sup>. A peculiar microbial cell covered with a membrane that protects it from noxious influences in the surrounding environment.

of a certain fungus were introduced into the body of a sea crustacean, the daphnia, a large number of cells concentrated around them catching and destroying the microbes and the daphnia remained well. Mechnikov named the cells destroying the microbes phagocytes (devouring cells) and the phenomenon of catching and devouring the microbes phagocytosis. Mechnikov proved that if an animal was infected with microbes covered with special protecting capsules that made them impervious to phagocytosis, the animals developed a fatal disease. At the same time the majority of microbes without capsules were quickly caught, (phagocytized) by the white blood cells, the infection could not develop and the animal remained well.

It must be noted that all the defense mechanisms of the organism beginning with the skin and mucous membrane and ending with the defensive properties of blood serum and the action of phagocytosis are in close relationship with all other vital functions of the organism and primarily with the metabolism and function of the central nervous system. It has been definitely established that starvation decreases the resistance of an animal to diseases to which it is immune when receiving sufficient nourishment. The resistance of an organism is drastically reduced when it is deprived of an adequate amount of valuable proteins (meat and fish). The defense forces of the organism are also lessened when the food is deficient in vitamins, especially A, B, C and D. Professor A.M. Kirkhenshtane and his co-workers gave numerous demonstrations of how the body resistance is lowered by a diet lacking in vitamins. Animals deprived of vitamins easily fall prey to diseases to which they are immune under normal conditions. Due to the well known works of the great Russian physiologist I.P. Pavlov and his many co-workers, it has become known and generally accepted that the functions of the organism are regulated by the nervous system. Recently it was proved that the defensive functions of the organism are also somewhat dependent on the condition of the nervous system. P.F. Zdrovskiy, for instance, proved that during sleep, artificially produced by drugs, the formation of defensive substances in the blood is inhibited and the defensive-inflammatory reactions limited. Other researchers proved that substances secreted into the blood during stimulation of certain segments of the nervous system (for instance, adrenalin, the hormone of the adrenal gland), increases the phagocytic activity of the leucocytes.

And so all these various defense mechanisms are closely related to each other and are directly related to the general condition of the organism, the state of metabolism and the functioning of the central nervous system.



All the above-mentioned defense mechanisms are present in every healthy organism. These mechanisms assure natural, i.e., not artificially induced resistance to certain infectious diseases in both man and animals.

The organism's capacity to resist the action of a particular disease-producing microbe is called immunity.

Many phenomena in the relations between the organism and microbes that appeared puzzling in the past became understandable after the rules of the activity of the defensive mechanisms were learned, particularly those related to the natural immunity of the organism to the action of certain microbes. For instance, it was known long ago that people did not contract certain diseases common to animals (for instance, chicken cholera, infectious anemia of horses, canine distemper etc; on the other hand, the animal does not contract typhoid fever, syphilis etc. It has become clear that all this is due to the natural immunity peculiar to the given species of animal or to man. The natural immunity of the species depends on the biological peculiarities of the given species or man. Besides the natural immunity of the species it is well known that some persons are resistant to some diseases owing to their peculiar individual properties. This is called the natural immunity of the individual. Individual immunity appears to be the reason that the most infectious diseases never afflict an entire population but always spare a portion of it. This explains the fact that some members of a family stricken with an infectious disease (for instance, smallpox plague) remain well in spite of being exposed to the disease.

Man and animals are born possessing natural group and individual immunity, therefore the group and individual immunity is also called natural inherent immunity. Besides the group and individual immunity there is also the inherited immunity of infants during the first months of life. The immunity of the newborn is due first of all to the inadequate development of certain sectors of their nervous system that remain insensitive to the action of the microbes and their toxins and secondly to the fact that temporarily present in the infant's organism are defensive substances received from the mother. This explains the fact that up to the age of six months infants almost never contract measles, scarlet fever and some other infectious diseases.

The acquired immunity to some diseases is different from the inherited. Man is not born with it, but acquires it during his life, usually as a consequence of having suffered some infectious disease. The immunity of man to a recurrence of the diseases that he had once had, is called infection-acquired natural immunity. The infection immunity has some

characteristics distinguishing it from the naturally inherited immunity. The main characteristic of the infection immunity is its specific nature, i.e., it is a type of immunity limited exclusively to the infectious disease that has been endured. Therefore the immunity acquired after measles prevents a recurrence of this disease, but not of pertussis, diphtheria etc.

At the core of group and individual natural immunity is the function of the previously described defense mechanisms possessed by every healthy man and animal. The acquisition of infection-immunity is accompanied by the appearance of new additional defense mechanisms that result in the destruction of the causative agent of this disease, assure the recovery of the organism and protect it from a recurrence of the illness in the future. The increase in the phagocytic functions of the leucocytes and the considerable increase in the ability of the serum to render the microbes and their toxins harmless are a part of these additional mechanisms.

The study of the serum of an immune, i.e., resistant organism, shows that it contains a large number of special defense substances called antibodies. The organism forms antibodies in response to the penetration of microbes and their toxins. The formed antibodies possess an amazing ability to combine with the microbes and their toxins and to neutralize them and render them harmless. By their nature the antibodies represent specifically changed macromolecular serum proteins--the globulins. The distinctive property of antibodies is that they combine with those microbes or their toxins that have caused the given disease and in response to whose attack on the body of these antibodies had become formed in the first place. The neutralization of the microbes takes place in various ways -- by agglutination, precipitation or lysis. As a result, the microbes and their toxins are rendered harmless.

In the serum of an immune animal there are special antibodies that prepare the microbes for phagocytosis making them easier to catch and digest. The markedly increased phagocytic capacity of the leucocytes in an immune organism is derived from the presence of these antibodies. The antibodies are present in a particularly large number at the termination of the disease and are preserved for a long time and in some diseases, for life. During this period the organism remains immune to a recurrent infection; thus, the infectious diseases of childhood such as measles, chickenpox, and mumps produce a lifelong immunity. People who were ill with typhus, tularemia and other infectious diseases remain immune to them for a long period of time.

Is it possible to impart artificially to an organism, making it unnecessary for it first to undergo infectious disease? Life itself has prompted the answer to this question.

Physicians noticed long ago that if a man was in contact with the sick and gradually infected with very small or weakened doses of microbes or their toxins, he remained well and after a time acquired a hidden, life-produced immunity. Thus under natural conditions man can become immune without having been sick! May it not be possible to reproduce this state under artificial conditions, by infecting a man with attenuated microbes or with very small doses of the infectious agent? Isn't it possible in this case to produce antibodies in the blood serum and make the organism immune without causing the disease? These ideas formed the ground work of prophylactic inoculation.

## THE HISTORY OF PROPHYLACTIC INOCULATIONS AGAINST INFECTIOUS DISEASES

Since ancient times there has been a tendency to deliberately infect people with a light form of diseases that in the opinion of the physicians of that period were impossible to avoid.

This was done to produce immunity and prevent serious forms of the disease.

About three thousand years ago Chinese and Hindu physicians were vaccinating patients against smallpox by rubbing into their skin dried up smallpox pustules obtained from the sick. In Europe and Africa the dried pustules were applied to incisions made on the skin. N.F. Gamaleya wrote that some Caucasian people used a needle immersed in the content of the smallpox vesicles to prick the skin of girls as a safeguard against disfigurement (smallpox frequently disfigures people for life). In the second half of the 18th Century the famous Russian scientist and epidemiologist D. Samoylovich tried to protect the population from a raging epidemic of the plague by injecting of pus taken from the suppurated lymphatic nodes (buboes) of a patient ill with the plague.

However, these attempts at artificial immunization were far from safe and sometimes ended tragically, the people becoming ill with a serious or fatal form of the disease.

The credit for devising the first scientific and highly effective form of vaccination belongs to the rural English physician Edward Jenner who was the first to produce a successful vaccination against smallpox. Jenner noticed that a person recovered from "cowpox" or "vaccinia" (from the latin word "vacca" -- a cow), becomes immune to the human pox. As cowpox



took a very mild form in man, Jenner decided to infect people artificially with cowpox, rendering them immune to the infection with smallpox. However, before putting his idea into practice, Jenner did a great deal of tedious work in experimenting with animals and checking the validity of his hypothesis. Only after 20 years, when he was sure of the complete safety of cowpox vaccination did he undertake the decisive experiment -- the vaccination of a man. The first vaccination was performed by this scientist on an eight year old boy, James Fibbon. Having obtained some liquid from the vesicles on the finger of a milk-maid infected with cowpox, he rubbed it into a scratch on the arm of the child. At the place of the vaccination there appeared initially, a vesicle filled with pus, then a crust that dried and fell off leaving behind it a small scar similar to those we now see on every person vaccinated against smallpox. To prove that the vaccination with cowpox prevented smallpox, it was necessary to try infecting the boy, showing that this attempt would be unavailing. Jenner took one more risk, and infecting the child with the pus of the human pox or as it was called "natural pox". [smallpox, M.E.]. The courageous researcher endured great anxiety before becoming certain that the boy would not become sick, proving that the experiment of artificial immunization was a success. This event took place in 1796, a year rightly called the birth year of artificial vaccines that, in years to come, protected millions of men from smallpox and eventually resulted in the speedy elimination of this disease in several countries.

The development by Jenner of a vaccine against smallpox and the inoculations against other infections developed later by his followers, have thus far been the greatest achievements of medical science and represent one of the most effective methods of controlling infectious diseases.

The consequent development of the science of inoculation is closely linked with the name of the French scientific genius and pioneer of microbiology, Louis Pasteur. He developed the method used today, of artificially attenuating the toxicity of disease-producing bacteria. Working with chicken cholera, Pasteur noticed that the bacteria left for a long time in the incubator (a special closet in which a uniform temperature necessary for the growth and multiplication of microbes is maintained) either completely lost their disease-causing properties or also caused a very light form of the disease in chickens. The most noteworthy fact that came to light in Pasteur's experiment was that the chickens that had suffered the light forms of the disease after being infected with weakened microbes remained well after being inoculated with fresh-grown microbes. At the same time

chickens inoculated with freshly prepared microbe cultures for the first time became sick soon thereafter and died. Pasteur's observations helped him to lay the groundwork for an entire series of experiments in which he incontrovertibly proved: first, that the toxicity of any infectious microbe can be artificially lowered to such a degree that the microbe loses the ability to cause disease, secondly, that inoculation of an animal with attenuated microbes will produce immunity.

Pasteur worked intensively on the method he had discovered of devising preparations for preventive inoculations against various diseases. The long and fruitful labors of this distinguished researcher yields preventive inoculations against anthrax and rabies. The latter inoculations were named after Pasteur and made his name immortal.

Microbiology, the science of microbes developed rapidly in the 80's and 90's of the past century. Each year brought new discoveries and by the end of the 19th Century the causative agents of leprosy, relapsing fever, dysentery, diphtheria, gonorrhea, tuberculosis, tetanus and many other infectious diseases were known.

The isolation of the causative agents of infectious diseases in a pure state opened up possibilities in the field of new preventive inoculations. Every year the number of diseases against which prophylactic inoculations were found became greater.

Wright in England, Pfeiffer in Germany, and Vysokovich in Russia had obtained good results from inoculations against typhoid fever as early as 1897-98. In the same years Shiga in Japan and Rozental' in Russia prepared and used a serum against dysentery. The pioneers of inoculation in Russia were N.F. Gamaleya and G.N. Gabrichovski. N.F. Gamaleya jointly with Ya. Yu. Bardakh has proved the entire safety and high effectiveness of inoculating against rabies on the basis of multiple experiments and observations of persons bitten by rabid animals. Their works have played a great role in defending Pasteur and his method of preventing rabies against attacks by his critics. A great role in the organization of prophylactic inoculations in Russia also belongs to G.N. Gabrichovski.

A great forward stride in the development of inoculation was the discovery of the attenuated toxin of diphtheria microbes by the French scientist G. Ramon. This was given the name of toxoid and proved extremely effective in preventing diphtheria.

As new vaccines were developed, the mechanism of their action was studied. It was discovered that in the blood serum of the inoculated as well as of persons that had had the

disease, there appeared a large number of antibodies able to render harmless the causative agent of the disease against which the individuals were inoculated. The phagocytary action of the white blood cells increased in the inoculated, i.e., the ability to seize and digest the causative agents of the given disease. It is easy to see that after inoculations, immunity to the disease developed as it did after an infectious disease. The only difference between them being the fact that in the inoculated the immunity appeared without any danger to the organism, whereas in persons who had been sick it was the result of the infectious disease. The immunity after inoculation was called artificially acquired immunity as distinguished from the naturally acquired immunity that comes from an infectious disease.

After establishing that a dominant role in controlling microbes and their toxins belongs to specific defensive substances -- antibodies found in the blood of inoculated individuals as well as in people who had had the disease, the researchers had a new idea: animals could be infected with certain microbes and made to produce defensive antibodies in their blood serum. Then this serum could be taken from the animal and used for the treatment of infectious diseases as well as the prevention of the disease in persons exposed to it. The first successful attempt to obtain a therapeutic serum was made in 1894 by the scientists Roux and Bering. They had been injecting the toxin of diphtheria microbes into horses and had found that this caused the formation of protective substances in the blood serum of the animals. The substances rendering the toxins harmless were called antitoxins, and the serum -- antitoxic serum. The use of the serum proved highly effective in the treatment of diphtheria. The mortality of the then-serious disease decreased more than 50 times due to the treatment with the serum. In Russia the first to use the antidiphtheria serum was G.M. Gabrichevskiy.

The serum containing antibodies against one or another causative agent was successfully used, not only for treatment but also for the prevention, of the disease in persons who were in contact with the patient and were under the danger of infection. The serum-prophylaxis is used extensively in preventing the measles. Owing to the fact that the absolute majority of the population had measles in childhood, the serum of the great majority of adults contains antibodies against the causative agent of this disease. The serum of people who had measles is effective in preventing measles in children who come in contact with the patient.

And so people become immune to diseases against which they were inoculated with attenuated or killed microbes or with serum.

The mechanisms of the action of inoculations and sera are different. When a vaccine is injected -- the organism itself actively produces immunity. Two to three weeks after the inoculation protective antibodies against the injected microbe appear in the blood. The immunity developed in the organism after the penetration of a vaccine is called active. In the case of serum, the organism receives ready-made antibodies, and does not take an active part in producing immunity. Therefore the immunity that is imparted to the organism by the injection of serum is called passive.

The active immunity differs from the passive in requiring several weeks to form, whereas, passive immunity is imparted to the organism within a few hours after the injection of serum.

In addition, active immunity continues for a time, years and sometimes decades; passive immunity is maintained only for two to three weeks after the injection of serum.

The administration of vaccines is prompted by other considerations than the use of sera: the vaccines are most frequently used when it is necessary to impart immunity that will protect the organism from infection for a long period of time. Sera are given when the person is already sick or has been exposed to infection and is in the incubation period of the disease, i.e., when it becomes necessary to take swift measures to render harmless the microbes and their toxins.

This is a kind of "first-aid" administered to the patient as treatment and to persons in contact with the patient, for the prevention of the disease.

The greatest forward strides in developing new and effective prophylactic inoculations were made by Soviet microbiologists after the great Socialist October Revolution. In a short period of time a number of effective preparations for inoculation were obtained, developed in industrial production and put to wide use. M.P. Pokrovskaya, N.N. Zhukov-Vereznikov and E.I. Korobkova obtained an effective vaccine against the plague. B.Ya. El'bert and N.A. Gayskiy developed an effective vaccine against tularemia, P.F. Zdrodovskiy and his co-workers are the discoverers of a vaccine against brucellosis, N.N. Ginsburg developed a vaccine against anthrax. M.K. Krontovskaya and M.M. Mayevskiy and also A.V. Pshenichnov submitted various vaccines against typhus. A.A. Smorodintsev, V.M. Zhdanov and other researchers were able to obtain an anti-influenza vaccine and serum which proved effective in preventing influenza. Back in the period of the Great Patriotic War, A.A. Smorodintsev, E.N. Levkovich and A.M. Shubladze developed methods for obtaining a vaccine against tick encephalitis, a serious and contagious disease of the nervous system.

Recently the Soviet scientists have successfully completed the work on vaccines against pertussis and epidemic infantile paralysis (poliomyelitis).

These successes in the development of effective vaccines and sera as well as the continuous new research in this direction open up great perspectives for the greater control of many infectious diseases.

### ORGANIZATION AND IMPLEMENTATION OF PROPHYLACTIC INOCULATIONS

We have already said that a vaccine is any preparation designed to produce an active immunity in the organism.

Vaccines could be live and killed.

The majority of live vaccines are attenuated microbes. It is possible in practice to deprive the microbe of its ability to produce a disease by infecting with it animals that are only slightly susceptible to it. For instance, the virus of human smallpox loses its ability to produce diseases in man after it has caused cowpox in a cow. Another way to weaken the ability of the microbes to cause disease is by acting on them with high temperatures, pressures and other physical factors (for instance, the vaccines against anthrax are prepared by this method, or by growing the microbes in the presence of chemical substances that decrease their activity, (this method is used for the preparation of a vaccine against tuberculosis).

Killed vaccines consist of microbes that were killed by heating, formalin, or other means. These are the vaccines used against typhoid, dysentery, cholera and some other infectious diseases.

Besides live and killed vaccines there are vaccines in use that consist of fragments of the microbial cells extracted by chemical means. To obtain these vaccines such component parts of the cells are extracted as are capable of creating immunity.

An example of such a vaccine is the polyvalent ("poly" means many) used for inoculation against several infectious diseases (typhoid, paratyphoid, dysentery, cholera etc.).

Whenever the main role in the development of the disease belongs not to the microbe, but to its toxins, as for instance in diphtheria and tetanus, the vaccine is made not from the microbe itself, but from its toxin. The toxins are rendered harmless by various chemical substances, such as formalin, that make them lose their toxicity. These are so-called toxoids, used in inoculations against diphtheria and tetanus.



The vaccine is introduced in the organism in various ways: subcutaneously and intradermally by means of a syringe, percutaneously by rubbing it into small cuts on the skin, by mouth and even into the nasal cavity. The majority of the vaccines are administered subcutaneously (for instance the vaccines against dysentery, typhoid, paratyphoid, cholera, typhus, diphtheria, tetanus, rabies and other diseases). In some cases attempts are made to inject the vaccine through the same route by which, under normal circumstances, infection takes place: for instance, the vaccine against influenza is introduced through the mucous membrane of the nasal cavity and so forth.

The majority of the vaccines produces immunity to the disease for a period of one to five years; hence, to obtain strong and lasting immunity it is necessary to repeat the injections several times. The first immunization is called inoculation, the second, re-inoculation. Inoculation can be highly effective only if the dates of inoculation are carefully observed. It is necessary to give repeated injections against smallpox, diphtheria and tuberculosis.

The organism responds to the injection of a vaccine with a general and local reaction. The local reaction produces redness, some swelling and sometimes slight tenderness at the place into which the vaccine was introduced (this reaction can occur only if a percutaneous, intradermal or subcutaneous method of introducing a vaccine is used). These phenomena at the place of injection are the usual reaction of the organism to the introduction of a vaccine; they last two to three days or somewhat longer and disappear without a trace. The systemic reaction is manifested by malaise and increase of temperature for one or two days. After some inoculations, the systemic reaction may resemble mild symptoms of the disease against which the injection was administered. For instance inoculation against intestinal infectious diseases may be followed by a mild diarrhea lasting for one or two days.

After most immunizations, most of the persons inoculated can continue to work. Only occasionally do malaise and elevated temperatures last several days. In these cases it is said that the reaction to the inoculation was pronounced. Persons suffering from a marked reaction are not permitted to do physical work after being inoculated and sometimes are told by the physicians to remain in bed for two or three days (until the reaction disappears).

It is important to note that even a strong reaction is completely safe and does not prevent immunity.

Every type of inoculation has its own indications and contraindications.

Indications for inoculation. Some inoculations are given to the entire population. These include vaccinations against smallpox. In other cases the inoculations are given to groups of the population exposed to some disease owing to specific conditions of work or the prevalence of a particular disease in a given area. For example, injections against brucellosis are given to veterinary workers, cattle breeders and other persons who are in constant contact with livestock affected by brucellosis who are the main source of this disease. Inoculations against tetanus are given to agricultural workers, persons doing earthwork, workers of the peat industry and other workers whose occupations make skin trauma and contamination of the wound with soil a possibility.

All these inoculations follow a plan established by the department of health. Unplanned inoculations are given on so-called epidemic indications, i.e., when there are occurrences of some disease in a district, or the district next to it and the danger exists of its being brought in and spread. For instance, if a few cases of tularemia appear in some area, the entire population must be inoculated against this disease. Such measures quickly check the outbreak. Immunizations on epidemic indications are conducted against typhus, anthrax and some other diseases.

Contraindications for inoculation are: febrile conditions and acute infectious diseases, as people affected with an acute infectious disease could have very strong reactions to the inoculation. It is clear that in such circumstances the inoculation could be postponed without any harm until the disease is over and full recovery has taken place. Some inoculations should not be given if active tuberculosis, severe forms of diseases of the kidneys, the liver and the cardiovascular system are present or in the second half of pregnancy.

Whether or not inoculation is desirable should be decided by a physician after proper examination of the patient.

However, there are diseases that constitute such a danger to life that in some cases inoculations against them are given independently of the state of health of the patient. For example, if there is danger of contracting smallpox the entire population is vaccinated against this disease without taking into account the state of health of some individuals.

Injections against rabies are also classified as immediately necessary. This disease is incomparably more dangerous than the strongest possible reactions to the vaccine in sick persons.

Some inoculations can be performed during any time of the year. These include injections against diseases that do



not have a seasonal peak of morbidity and that have been eliminated in our country (for instance smallpox). Some infectious diseases tend to increase during a certain period of the year. For example, it is well known that gastrointestinal diseases occur mainly in the Summer and Fall, and influenza in the Spring and Winter. Therefore, inoculations against diseases with a characteristic seasonal prevalence should be carried out before the seasonal peak of morbidity to give the public an adequate, immunity well in advance of the time at the greatest incidence of the disease. This is why inoculations against intestinal infections are given in April through July and against influenza in September through November. If the incidence of a particular disease increases the inoculations against it are conducted independently of the season of the year.

Vaccines will be discussed individually in the next chapter of this brochure.

Let us discuss the general importance of prophylactic inoculations.

Not all inoculations confer the same degree of immunity from disease or, as it is customary to say, different vaccines possess a different effectiveness. Some vaccines are highly effective; the administration of these vaccines virtually excludes the possibility of the inoculated person contracting the disease; The vaccine against smallpox is in this category. As it is known, the compulsory smallpox vaccination of the entire population in our country has totally eliminated smallpox. Equally effective is the vaccine against rabies, whose timely administration gives full protection. The vaccines against tularemia, diphtheria and many other infectious diseases are highly effective. Prophylactic inoculations are the leading measures in controlling these diseases.

In some infections the inoculation does not protect all inoculated persons from the disease. However, the effectiveness of these vaccines lies in the fact that the vaccinated persons contract the disease less frequently than the nonvaccinated, and if contracted, its course is much milder and never fatal. Vaccines that decrease the morbidity among the inoculated, but do not completely protect them from the disease are as follows: Inoculations against typhus, typhoid, paratyphoid and some other diseases. Therefore, prophylactic inoculations against typhoid and paratyphoid have a secondary importance in controlling these diseases, the main role belonging to timely diagnosis and treatment and to preventive measures of personal and communal hygiene that check the spread of the disease.

## INOCULATION AGAINST THE PRINCIPAL INFECTIOUS DISEASES

In spite of the fact that smallpox, diphtheria and tuberculosis are completely different diseases, the aims and the organization of preventive inoculations against them have much in common: 1) all these inoculations are compulsory for the entire population; 2) they all begin in early childhood; 3) to obtain a reliable and permanent immunity these inoculations should be repeated three or four times; 4) most of the successive inoculations against the above infections are given to children of preschool and school age, and therefore cooperation between the school and the department of health is an important factor.

Inoculation against diphtheria. Was there ever a mother that did not fear the dreadful word "diphtheria"!! Was there ever a parent that did not hear about the dense diphtheria membranes that plug up the respiratory tract of the child, causing asphyxia!! The suffering of the asphyxiating child, the emergency tracheotomy operations, sometimes ending fatally, such was the old picture of this once dreaded infection that took thousands of children's lives.

Diphtheria has been known to man since antiquity. Epidemics of diphtheria were constantly breaking out in various parts of the world. The incidence of the disease increased greatly between 1860 and 1880, when diphtheria spread throughout the entire world, not sparing even such remote areas as the Pacific Islands and Australia. In Russia diphtheria occurred constantly from the middle of the 19 Century; from 1886 to 1912 more than six and one-half million cases of this disease were reported. At that time diphtheria had a very severe form; it ended fatally in about 50 percent of the cases. The prevalence of diphtheria, its severity and high morbidity, commanded the constant attention of researchers.

The first great success in the control of diphtheria was achieved in 1894 when the scientists Roux and Bering obtained antidiphtheria serum and used it in the treatment of diphtheria. The use of serum in the treatment of diphtheria proved effective; however, morbidity remained high and the form severe. The scientists continued to search for ways and means of preventing diphtheria. Their search was crowned with great success.

As a result of long and determined work the French scientist G. Ramon succeeded in obtaining an effective preparation for immunization against diphtheria. He was able to obtain an attenuated toxin of the diphtheria microbes -- the toxoid.

The diphtheria toxoid was originally tried in experiments on animals. It showed that the animals tolerated the vaccination with toxoid well and that antitoxins formed in their blood were able to render diphtheria toxin harmless when given to patients who had contracted this disease. In 1923 experiments on men with the diphtheria toxoid began. From the very first, it became apparent that this preparation gave medicine a powerful weapon for controlling diphtheria. The morbidity among the inoculated dropped markedly, and when the disease occurred it ran a much milder course and was almost never fatal. In France, for instance, the diphtheria morbidity averaged about 20 thousand yearly from 1919 on. In 1951, after wide use of the vaccine the number of cases dropped to 2689 yearly, and the mortality for the same period of time decreased from 2200 to 135 cases per year.

In summarizing the results of inoculations against diphtheria G. Ramon wrote in 1956 in the Soviet "Journal of Microbiology, Epidemiology and Immunobiology" that owing to inoculations against diphtheria, "this disease once so dreaded by mothers and until recently the cause of many worries to the practicing physician, has become but unpleasant memory".

The immunization with diphtheria toxoid requires two inoculations and three re-inoculations. The vaccine is given the child at the age of five or six months. It consists of two injections of the toxoid at an interval of three to four weeks.

In some cases this interval could be prolonged to one and a half months.

The diphtheria vaccine is again given the child at ages one, three, seven and twelve. The first booster shot should take place six to twelve months after the second injection i.e., after the inoculation had been completed. It must be remembered that the original inoculation, unless followed by successive shots, does not give sufficient immunity; only a rigorous observance of the dates of inoculation can give children a lasting and reliable immunity to diphtheria.

If children who had been given the vaccine do occasionally get sick, the disease is mild and does not leave any complications.

The Soviet Union has long been giving compulsory inoculations against diphtheria to children. The rate of this disease in our country annually decreases. When it occurs, it is much milder than in the past, complications are less common and a fatal outcome is extremely rare.

And if diphtheria still occurs in some of our cities, it is due only to the inadequate scope of primary and especially secondary inoculation of the entire child population.

The giving of shots to every single child in the country and compulsory compliance with the exact dates of re-inoculation are basic measures in controlling diphtheria.

Inoculation against tuberculosis. Control of tuberculosis has always been a problem of tremendous social importance. It is well known that the spread of this disease is aided by difficult economical conditions, poor nourishment, and poor living and working conditions. This is why tuberculosis is particularly common among the workers in capitalist and colonial countries. In the Soviet Union a vast system of social measures aimed at the improvement of the working and living conditions of the people helps control this disease. For many years efforts to find a vaccine against tuberculosis have been unavailing. The main difficulty lay in the fact that killed microbes did not produce immunity to tuberculosis. Inability to give the organism immunity against tuberculosis by injecting killed tubercular microbes was related by the peculiarities of immunity to this disease. As a result of many years of work the French scientist Calmette succeeded in learning the nature of immunity in tuberculosis. Calmette proved that immunity to tuberculosis continued as long as the causative agent remained in the organism. The microbes had to be live but so few and so weakened that they were not able to suppress the defensive agencies of the body.

Thus, to obtain immunity to tuberculosis it would be necessary to introduce live microbes into the organism. But in doing this how could infection be avoided? It is dangerous to introduce live tuberculosis microbes even in very small doses. It was necessary to achieve such changes in the tubercular microbes as would make them unable to cause the disease, while preserving the capacity to produce immunity. Calmette and Guérin started their experiments more than 40 years ago choosing microbes of bovine tuberculosis as the least infectious for man. To attenuate these microbes Calmette grew them on special nutritive media for 13 years, reculturing them every 15 days onto a new medium. After four years these microbes lose their capacity to produce tuberculosis in cattle and after a few more years they prove harmless to other animals as well.

Extensive observations have proved that the microbes of Calmette and Guérin (or as they are called, the bacilli of Calmette and Guérin) are innocuous and never become more infectious. The vaccine prepared by these scientists is called B.C.G. (the first letters of the Latin words Bacilles Calmette-Guérin).

The first time BCG was given to man was in July 1921. Henceforth it was universally recognized. Since children may

become infected with tuberculosis even in infancy, and most often the mouth, Calmette suggested that his vaccine be taken by mouth in mother's milk a few days after birth.

In the Soviet Union as well as in several other countries the tuberculosis vaccine is given to all newborn infants.

The first tuberculosis vaccine is given on the third, fifth, and seventh or the fourth, sixth and eighth or the fifth, seventh and ninth day after birth. The child is given two ml of the vaccine mixed with breast milk. Repeated inoculations against tuberculosis (re-inoculations) are given by the percutaneous method. The re-inoculation against tuberculosis is given to children two to seven years of age and then in the fourth, seventh and tenth year of school. The skin of the upper arm is cleaned with alcohol or ether, after which drops of the vaccine are put on the dry skin. Slight superficial scratches are made through each drop and the vaccine is rubbed in. The place of inoculation is covered with sterile gauze and wax paper and then bandaged for an hour, after which the dressing is removed. The inoculation is considered completed. Soiling of the inoculated spot should be avoided. After 48 hours medical personnel check on the results of the inoculation. If immunization has taken effect, a dry crust will have formed over the scratches two days later. In the absence of this it is considered that the inoculation has been improperly performed and the vaccine has not taken. In such cases inoculation should immediately be repeated.

Immunization against tuberculosis is an effective measure in controlling this disease provided the dates of vaccinations are adhered to and the entire child population is immunized.

Vaccination against smallpox. Smallpox vaccinations introduced by Jenner 150 years ago made possible the complete elimination of this disease in many countries starting with the USSR. In our country the first decree on compulsory smallpox vaccination was signed by V.I. Lenin of 10 April 1919. Since then smallpox morbidity has rapidly declined and in 1936 smallpox was completely eliminated throughout the territory of the USSR.

Up to now many countries including Britain, the country in which smallpox vaccination originated have no law on compulsory immunization against smallpox. As a consequence of this thousands of people annually are stricken with this disease in many British colonies.

Many cases of smallpox are also observed in Britain itself.

The technique of vaccination against smallpox differs little from re-inoculating against tuberculosis. Since the



spot vaccinated may become itchy and children tend to scratch it, children's nails should be cut before vaccination. The skin at the place of the vaccination (the upper arm) is also cleansed with alcohol or ether. When it is dry, three drops of the vaccine are put on the skin. A single superficial and non-bleeding incision is made through each drop with a special instrument for smallpox vaccination (lancet). It is not necessary to rub in the vaccine. The surface of the skin at the point of vaccination is left uncovered for several minutes. After seven or eight days medical personnel checks on the results of the vaccination. The vaccination is considered successful if at least on vaccinid, representing a vesicle filled with pus appears. If the smallpox vaccine did not take, vaccination should be repeated. The vaccinid should be protected from trauma and should not be moistened during a bath. Should the vaccinid become traumatized or any complications develop a physician should be consulted.

Primary and secondary inoculations against tuberculosis, smallpox and diphtheria should be correctly alternated.

The Ministry of Health USSR has worked out the following chart of immunization dates.

The first BCG vaccine is given the newborn in the maternity hospital. The diphtheria anti-toxin is given from the fifth to the sixth month of life followed by vaccination against smallpox at the age of nine to ten months. Repeated inoculations are administered to children at the following ages:

Type of inoculation	First inoculation	Second inoculation	Third inoculation	Fourth inoculation	Fifth inoculation
BCG (against tuberculosis)	2 yrs	7 yrs	4th grade	7th grade	10th grade
Against smallpox	4 yrs	8 yrs	12 yrs	18 yrs	---
Against diphtheria	1 yr	3 yrs	7 yrs	12 yrs	-----

Thus, most of the inoculating fall to children of school age. This emphasizes the importance of cooperation between school authorities and the department of health. The school should help prophylactic immunizations by providing information on sanitary methods to students and parents and by organizing inoculation centers in schools.

A non-inoculated child could have serious complications from diphtheria. Recently, this happened in the family of a teacher. Two of the teacher's children, aged three and four and a half attended kindergarten. It happened that the older child was absent from school at the time of immunization against diphtheria, the mother refused, under various pretexts, to give him his shots in spite of the fact that the kindergarten physician repeatedly reminded her of it.

The child began ailing. He was listless and cranky, refused food and complained of pain in the throat on swallowing. His temperature rose to 38.5°. The physician diagnosed a severe form of diphtheria. In the unprotected (not immune) organism, cardiac complications soon set in. All the efforts to help him failed and he died shortly thereafter.

The disease, its severe form and fatal outcome were all largely due to the fact that the child had not been immunized against diphtheria and had no protection against the infection.

This short example is a convincing demonstration of the value of timely inoculation of children against diphtheria and of the serious and even fatal consequences that could result from neglect of this tremendously important prophylactic measure.

Inoculation against pertussis. [whooping cough] Pertussis is second only to measles, as far as frequency of its occurrence is concerned. Susceptibility to pertussis in children is very great and, compared with other infections, it afflicts a greater number of children between the early ages of one to five.

Pertussis does not spare children during their first month or even during the first days of life.

The source of infection are sick children especially during the first and second weeks of the disease. The causative agent (bacillus pertussis) is expelled by the patient in droplets of saliva and mucous while coughing. Infection with pertussis occurs from prolonged and close contact with the patient. The bacillus of pertussis perishes rapidly outside the body and therefore pertussis is not transmitted through a third person or through toys or other objects.

The disease starts with an increased temperature and recurrent cough. The attack of spasmodic coughing (and whooping) consists of several successive cough impulses.



It lasts from one to two minutes and ends in a thick viscid expectoration and sometimes in vomiting. The attacks of coughing traumatize and upset the child. During the attack the circulation and respiration are interfered with. Pertussis by itself can be very severe, especially to small children. In addition, the disease may be complicated with serious and prolonged pneumonia and dilation of the bronchi (bronchiectasy). In some cases meningitis may develop. The wide use of new and effective antibiotics in pertussis (synomycin, levomycetin, biomycin) has led to a great decrease in the number of complications and also a marked decline in mortality. The pertussis morbidity has not changed and pertussis remains a prevalent infectious childhood disease.

It is known that pertussis gives strong, lifelong immunity. This fact, has touched off the search for prophylactic shots against pertussis. Work in this direction was conducted quite successfully in the last five to seven years in the USSR as well as abroad. As a result, effective vaccines against this disease have been obtained. The vaccine consists of a suspension of pertussis microbes rendered harmless by formalin. It is injected subcutaneously in the amount of one ml.

Three shots are given, at three to four week intervals.

All children up to the age of five inclusive are inoculated against pertussis as they are the age group most susceptible to this infection. Older children are given shots only if there is a rise in the incidence of whooping cough.

Children who had been inoculated contract pertussis only one twelfth times as often as the non-inoculated. Inoculation of children who have come in contact with pertussis patients protect them against it. In the rare cases of children becoming ill after the first and second shot when insufficient immunity had been obtained, the disease is very mild and without complications. The immunity after the inoculation develops so rapidly that it is expedient to give the vaccine (in small doses) at the onset of the disease to hasten the development of immunity as well as the recovery. Thus the vaccine against pertussis has not only prophylactic, but also therapeutic properties.

The pertussis vaccine is given at the same intervals as the diphtheria vaccine (i.e., at the age of five to seven months, one year and three years). Shots against pertussis are given to children that were previously immunized against diphtheria. The vaccine is administered three times at two to four week intervals. Re-inoculation against pertussis is done with the pertussis-diphtheria vaccine at dates set for diphtheria re-inoculation. Because the dates of pertussis

and diphtheria coincide, the development of a combined (or associated) pertussis-diphtheria vaccine, containing killed microbes of pertussis and diphtheria toxoid is of great importance. The pertussis-diphtheria vaccine is given on the same indication as the separate shots against diphtheria and pertussis. The creation of a package pertussis-diphtheria vaccine makes the work of immunization much easier.

Inoculation against poliomyelitis. (Infantile Paralysis) Infantile paralysis or poliomyelitis is a dangerous infectious disease which produces paralysis of the facial nerve, muscles of the hands, legs and other parts of the body. At times this disease involves the respiratory muscles with very serious and often fatal consequences. Even after recovery the patients quite often remain paralyzed. The danger and seriousness of this disease made it necessary to develop a vaccine against poliomyelitis.

The basis for all the work in the development of a vaccine against poliomyelitis was the research by Enders who succeeded in growing the virus -- a minute microbe, which is the causative agent of this disease -- outside the living organism on artificial nutritional media (human embryonic tissue). After this discovery the so-called simian period of poliomyelitis, when these expensive and often unavailable animals were required for the experiments came to an end. The practical importance of Ender's discovery was that it made it possible to obtain the causative agents of poliomyelitis in an unlimited quantity necessary to the production of a vaccine. On the basis of Ender's method in 1953, Dr. Salk developed the technique of multiplying the virus and rendering it harmless by formalin. A killed vaccine against infantile paralysis was obtained. At the present time over 40 million people were inoculated with this vaccine in the US, Canada, France and other countries. The vaccinations do not give complete protection against the disease, however, their efficacy is unquestionable: among the inoculated the morbidity is markedly decreased, particularly with regard to the severe paralytic forms; besides, no mortality is observed among the inoculated.

Salk's vaccine contains the killed virus; however, as was long known, the best effect is obtained from immunizations with live vaccines which the scientists are always endeavoring to obtain. Efforts to obtain new attenuated vaccines against infantile paralysis did not cease. Finally Albert Sabin succeeded in obtaining the vaccine from the live attenuated virus of poliomyelitis.

The first results of immunizations with this vaccine indicated that it established the most reliable immunity.<sup>5</sup>

The Soviet researchers have been very successful in producing a vaccine against poliomyelitis. They have mastered the method of obtaining this vaccine and have organized its production. There is a special institute of poliomyelitis drugs in the Soviet Union, whose basic task is the preparation of poliovaccines. The vaccine produced by this institute contains either the one most frequently encountered type of virus (monovaccine) or all three known types of the causative agent of this disease (I, II, III).

The poliomyelitis vaccine is administered subcutaneously or intradermally. To obtain antibody levels in the blood in a quantity sufficient to give protection against poliomyelitis, the shots are given three times. The first two shots are given two to six weeks apart and the third, six to seven months after the second. For each subcutaneous injection, one ml of vaccine is required, for the intradermal -- a much smaller quantity (0.1 - 0.15 ml). The immunity after a full course of inoculations lasts not less than a year. At the conclusion of this period, it is essential to give one booster shot, which considerably strengthens the immunity.

Inoculations against poliomyelitis are given to all children in the most susceptible age group (from six months to six years).

In the future, it is planned to immunize all children up to age twelve.

Inoculation against poliomyelitis are an important measure in controlling this severe infectious disease of the nervous system. Special observations on the effectiveness of the immunizations made in the USSR, in the People's Republic of Rumania, in France and other countries, indicate that the vaccine gives protection against severe forms of the disease. Immunized persons have one-fifth of the morbidity of the non-immunized. The immunized hardly ever contract paralytic polio and their illness never has a fatal outcome. More than two million children were inoculated simultaneously by the intradermal method in May 1957, in the People's Republic of Czechoslovakia. In 1957 prophylactic inoculations against poliomyelitis by the intradermal and subcutaneous methods were successfully carried out in the Soviet Union, in Moscow, Riga and other cities. The development of prophylactic immunizations against infantile paralysis and their establishment in medical practice mark an important stage on the road toward the elimination of this severe disease.

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5. In the USSR a live, attenuated vaccine was also recently obtained. It is administered by mouth and creates reliable and lasting immunity.

Inoculation against the measles. The measles are the most common childhood disease. The causative agent of the measles is a filterable virus -- an unstable microbe that perishes almost instantantly outside the body. Therefore, the measles patient can be a source of infection. The incubation period lasts ten to twelve days after which the clinical picture, well known to every mother, appears. The child's temperature rises rapidly, the conjunctivae become inflamed, the eyelids puffy, lacrimation, cough, running nose and symptoms of inflammation of the mucous membranes of the mouth and respiratory tract appear. On the third or fourth day a macular eruption appears, first on the face and then the skin of the trunk and the extremities. The eruption has a bluish tinge, is slightly elevated over the surface and spreads over the unchanged skin. At the time of eruption the patient is usually seriously ill; the child is listless and depressed. The eruption gradually pales and at the same time the temperature drops, however, this does not mean that the child has fully recovered: for a long time after this disease he will be sensitive to unfavorable factors in his surroundings (colds, infectious etc.). The measles greatly decreases the resistance of the organism to infection and children convalescing from the measles can easily contract scarlet fever, diphtheria and dysentery. In addition, the measles may aggravate tuberculosis, rheumatic fever and chronic dysentery. During convalescence various complications may arise. The most frequent and dangerous of them is pneumonia.

The measles gives permanent immunity and hence the production of an effective vaccine against this disease is, in principle, possible.

In recent years Soviet scientists have made definite forward strides in developing a vaccine against the measles. At the present time these vaccines are undergoing special tests and it is likely that they will be effective in helping control this disease.

At the present, protection against the measles is achieved by means of an antimeasles serum containing antibodies that render harmless the measles virus. This serum is prepared from the blood of adults on the assumption that all or practically all adults have had this disease.

The serum is made from the blood of donors or from blood collected in maternity hospitals from the placenta of parturients (so-called placental blood).

The antimeasles serum is given to all children between the ages of three months and four years (and older children if they are sick or in poor health) or exposed to the disease.

These measures are effective if undertaken not later than seven days after exposure to infection. To prevent the measles it is usually enough to inject 30 ml of the antimeasles serum intra-muscularly.

Immunity after these injections lasts only one month. During this period the vaccinated usually do not become sick, but if they do, the disease is insignificant and without complications.

In addition to the antimeasles serum, a special preparation, gamma globulin, is used for the prevention of the measles. It is obtained from whole human serum by extracting the proteins containing antibodies against measles. The advantage of gamma globulin over the antimeasles serum is that it has a higher concentration of antibodies against measles. Owing to this, a much smaller quantity of gamma globulin than of antimeasles serum is needed to prevent the disease (3 ml of gamma globulin instead of 30 ml of serum). The tolerance to gamma globulin is very good, there are no contraindications to its use.

Owing to the fact that protection lent by the antimeasles serum or gamma globulin lasts only 30 days, immunizations with these preparations cannot cause a marked reduction in measles morbidity. The main purpose of the seroprophylaxis of measles is to prevent its occurrence in small children who were exposed to it and in whom the disease takes a much more severe form than in older children.

Inoculation against the infectious diseases of the intestinal tract. The infectious diseases of the intestinal tract includes several diseases with a number of common symptoms. For instance, these diseases occur when microbes enter the intestinal tract with food or water: the greatest number of microbes is contained in the intestinal tract and is excreted with the feces. Finally, the spread of these diseases is directly related to the sanitary conditions of residential areas and the personal hygiene of the population (this is why prophylactic inoculation plays a secondary role in the control of infectious diseases of the intestinal tract). Some intestinal infections for instance, the cholera, have been completely eliminated in our country: the incidence of other intestinal infections (typhoid and paratyphoids) has been markedly decreased. Of foremost practical importance today is control of dysentery which is more widespread than any other intestinal infection.

After convalescence from dysentery the immunity is short-lived, hence infection with dysentery can occur after prophylactic inoculation, although the morbidity is less than among the non-vaccinated.



Moreover, a less severe form of the disease is observable in inoculated persons.

At the present time killed vaccines containing microbes against several intestinal infectious diseases are used to prevent dysentery. The most frequently used is the so-called tetravaccine (tetra -- four) which contains killed microbes of typhoid fever, paratyphoid and two of the most widespread causative agents of dysentery (microbes of Flexner and Sonne). Inoculations against the intestinal infectious diseases are frequently combined with tetanus toxoid (attenuated toxin of the microbes of tetanus). To prevent the intestinal infections and tetanus, a polyvalaccine is employed (poly -- many), containing six types of killed microbes (typhoid fever, two types of paratyphoid, two types of dysentery and cholera) and tetanus toxoid. The tetravaccine and the polyvalaccine are administered subcutaneously.

The immunizations against the intestinal infections are performed in the second quarter of the year (April through June) before the summer and autumn increase in morbidity, usually observed in a moderate climate. The tetravaccine is administered three times at ten day intervals. The tetanus toxoid is given simultaneously with the first and third injection.

The polyvalaccine is administered once. In the second and third year, the inoculation with tetravaccine and tetanus toxoid or with polyvalaccine is repeated.

Immunizations against the infectious diseases of the intestinal tract follow a previously established plan. The population of cities and rayons is inoculated if there is a rise in the incidence of typhoid and dysentery. People subject to resettlement are inoculated according to plan before their departure for their new homes or after their arrival there; this also applies to workers on construction projects, in the peat and timber industry, to plumbers and sewer workers, sanitation department employees, persons employed in laundries, the food industry, and restaurants, railroad and medical personnel, etc. If there are recurrent cases of typhoid or dysentery in a certain district, city or group (for instance, a factory, or dormitory all persons that are under threat of infection may be inoculated against these diseases.

Immunizations against intestinal infections usually have no ill effect and after taking the vaccine most people have no trouble working.

Contraindications to these vaccinations are acute febrile diseases and serious chronic diseases of the internal organs.

Bacteriophage is widely used in the prophylaxis of infectious diseases of the intestines. In 1889 the Russian scientist N.F. Gamaleya called attention to the fact that old cultures of microbes of anthrax contain some substance able to produce lysis of fresh cultures of this microbe. Later on D'Errel studied this phenomenon in detail on dysentery microbes. He established that during dysentery a substance able to produce the lysis of dysentery microbes appears in the intestine of the patient. This substance was named "bacteriophage" (the devourer of bacteria.). At the present time it is believed that the bacteriophage is a live protein substance. Its ability to destroy microbes has been put to practical use in combatting infectious diseases. Bacteriophage is grown in large quantities and is used internally against the microbes of dysentery or other intestinal infections, to cause their lysis and destruction. Bacteriophages are used most frequently against dysentery, typhoid fever and cholera. They are prescribed for persons who are in contact with the sick and consequently exposed to the danger of infection.

Bacteriophage is a liquid taken by mouth three times at five to seven day intervals. A single dose consists of ten ml of bacteriophage mixed with a tablespoon of a 5 percent solution of sodium bicarbonate (sodium is given because the gastric juice may destroy the phage). There are no contraindications to the administration of phage.

At the present time an intensive search is going on for attenuated vaccines against infectious intestinal diseases. It is hoped that these vaccines will be more effective than the killed vaccines now being used.

Inoculation against brucellosis. Livestock, including pigs, is the most common source of infection with brucellosis. Hence, the disease is primarily an occupational ailment of veterinary workers and workers of the livestock industry. This disease is transmitted through meat and dairy products obtained from sick animals and untreated with high temperatures (boiling, cooking and so forth).

Brucellosis is a lengthy disease (up to two years and more). Its symptoms are fever, profuse sweating, pains in the muscles, bones and joints as well as serious lesions of the nervous system, internal organs, sexual organs and the weight-bearing and motor apparatus.

Neglected and untreated cases may cause disablement.

Although brucellosis has become known to physicians relatively recently (about 70 years ago), not only the symptoms, diagnosis and treatment of this disease have been learned but specific prophylaxis by means of a live vaccine



consisting of attenuated microbes has been discovered. The credit for obtaining the vaccine against brucellosis goes to P.F. Zrodovskiy, P.A. Vershilova and other Soviet researchers.

The vaccine against brucellosis is a dehydrated suspension prepared from live attenuated microbes. Before the injection, it is diluted with a physiological solution (0.85%) of sodium chloride and is administered subcutaneously. Another vaccine is given percutaneously.

The inoculation very rarely results in a rise in temperature and malaise. Immunity to brucellosis appears within one or two months after the vaccination and is quite prolonged. After one or two years the vaccination is repeated.

Protection against brucellosis is given persons who come in close contact with sheep, cows and pigs among which cases of brucellosis had been observed. The vaccine is given to persons who tend livestock sick with brucellosis, to workers of slaughterhouses and meat producing factories, brinza (goat cheese, W.E.) factories, veterinarians and farm hands employed at farms in which some animals had been infected. No vaccinations are given to people ill with brucellosis in its clinical or latent forms.

Immunizations with the brucellosis vaccine are one of the basic means of preventing brucellosis among the population exposed to the infection.

Inoculation against tularemia. Tularemia was known in detail by 1912, at a later date than brucellosis. The source of this disease are several types of rodents: various breeds of mice, rats, hares, ground-hogs, water-rats and others. The infection with this disease can take place via various routes: by inhaling the microbes present in dust particles during harvesting, using food products contaminated by the feces and urine of mice and rats, bathing in water contaminated by infected water-rats, processing of the furs of sick animals and finally after being stung by insect vectors of the disease. The symptoms of the disease are a high temperature and inflammation of the lymph nodes, called tularemia bubos. The latter may suppurate and open resulting in ulcers which fail to heal for long periods of time.

Tularemia is a very contagious disease and under certain conditions can effect a large number of people very rapidly. Convalescence from this disease is marked by great weakness, and a lengthy loss of ability to work.

The vaccine against tularemia was obtained by the Soviet scientists N.A. Gayskiy and B.Ya. Elbert who succeeded, by lengthy reculturing, to attenuate the microbes of tularemia to such a degree that they lost the capacity to cause disease.

From these microbes, Elbert and Gayskiy prepared a live, attenuated vaccine against tularemia. Their vaccine proved effective but it had the disadvantage of being perishable. Faybich has improved this vaccine and prepared it in a dry form. The live, dry tularemia vaccine can be preserved for a long time. Tests of this vaccine have shown it to be highly effective.

Vaccinations against tularemia, as against smallpox, are performed by the percutaneous method. The skin is wiped with alcohol, a drop of the vaccine is deposited, superficial cuts are made and the vaccine rubbed into them. After the vaccine has been rubbed in, it should be allowed to dry for ten to fifteen minutes. The immunity developing after the inoculation affords reliable protection against the disease and lasts not less than five years and often considerably longer; moreover, the vaccinations practically never evoke a reaction (with the exception of people who had tularemia and who are excused from the vaccinations.) At the slightest hint of a tularemia epidemic, vaccination against it is given to the entire population starting with children aged four years.

In areas where cases of tularemia were observed in the past the vaccine is given the entire population (with the exception of children under four years of age). Scheduled vaccinations are also performed on all agricultural workers and industrial workers who process agricultural raw products such as grain, straw, animal feed and sugar beets. In addition, the vaccine is given people traveling to areas in which cases of tularemia have been reported, hunters for water-rats, skins, workers of plants where the primary processing of fur takes place and medical personnel who come in contact with tularemia patients. Immunizations are also given to people who come in contact with sick animals, but have not yet had any symptoms of the disease, because immunity after vaccination develops in less time than the incubation period of the disease.

Inoculations against tularemia at close intervals are a reliable guarantee of a rapid elimination of the disease.

Inoculation against anthrax. The source of anthrax are various animals; cows, sheep, horses, goats and buffaloes and also camels, pigs, cats, dogs, and hares. People get infected with this disease most frequently while working on the carcasses of animals that died from anthrax or while caring for sick animals. A so-called anthrax carbuncle forms at the place of penetration of the anthrax bacillus, presenting a blackish-brown crust under which purplish edema of the tissues has developed. It is hard on palpation and entirely insensitive even to needle pricks. If a person becomes infected

through the ingestion of infected meat or milk, he becomes sick with the intestinal form of the disease, which presents the clinical picture of strong abdominal pain, liquid bowel movements with an admixture of mucous and blood and symptoms of severe toxicosis. When the microbes enter the respiratory tract, the pulmonary form of the disease develops. It is characterized by chest pain, a strong cough, and copious secretions of liquid, blood tinged sputum. The intestinal and pulmonary forms of the disease are very severe and may have a fatal outcome.

The causative agents of anthrax can be preserved for years in the ground, feces and water. Even when heated over 140 degrees, the microbes of anthrax perish only after two to three hours. Neither does the tanning of the skins and salting of the meat kill them.

The above-mentioned circumstances have always drawn researchers to the problem of anthrax prevention. Louis Pasteur was the first to successfully achieve attenuation of a culture of anthrax microbes and to prepare a vaccine. Immunity after Pasteur's vaccination lasted one year. Our native microbiologist L.S. Tsenkovskiy has obtained, independently from Pasteur, a vaccine against anthrax that has several advantages over Pasteur's vaccine. Tsenkovskiy's vaccine is still used in veterinary practice. Recently, Soviet scientist N.N. Ginsburg succeeded in obtaining a new anthrax vaccine prepared from microbes that have permanently lost the capacity to form spores and cause disease. The Ginsburg vaccine has a high effectiveness. Its administration does not cause a reaction. This vaccine is given percutaneously (similarly to smallpox vaccination). After two or three days, small crusts are formed at the place of inoculation, which soon fall off. The inoculation is given only once. Should the need arise, another vaccination is given after one year.

At present, planned inoculations against anthrax are given people working wherever animal raw products are processed, especially wherever the processing of skins and wool takes place; it is also given to workers at meat factories. In areas in which there had been occurrences of anthrax among animals or in which there were actual cases of the disease among people, immunization is given to persons who come in contact with the livestock.

Inoculation against rabies. Rabies or hydrophobia is a disease of all warm-blooded animals without exception, including birds. Man becomes infected with this disease as a result of a bite by a sick animal or when its saliva falls on a skin wound. The importance of shots against rabies can be seen from the fact that until the discovery of the vaccine rabies was fatal: however, after the discovery of these vaccines, timely vaccination of bitten and infected persons

gives complete protection from the disease. The extremely rare cases of rabies that do occur are never due to the inadequate effectiveness of the immunization. The disease is always related to overlooking the danger of a bite or exposure to the saliva of sick or strange animals, and it never develops unless the vaccine was either not given or else given very late. Only a full course of injections given consecutively under the supervision of medical personnel is a reliable guarantee against rabies. The slightest laxity or irregularity of the person undergoing shots holds the great danger of succumbing to the fatal disease.

N.F. Gamaleya organized the first Pasteur station in Odessa 70 years ago. At the present time the USSR has more than 60 Pasteur stations and a large number of vaccination points stocked with a constant reserve of vaccines against rabies. This vaccine consists of an emulsion of the spinal cord of rabbits artificially infected with rabbits. To attenuate the causative agent present in the spinal cord, it is either dried, strongly diluted or treated with various chemical substances. The vaccine should be promptly given at the nearest Pasteur station, not only to persons bitten by animals known positively to be sick or by animals that may be sick, but even by animals that appear to be healthy. Persons who have scratches on their skin or mucous membrane of the eye, nose or lips made by nails of animals should go to a vaccination center. It is also necessary to see the specialist at the vaccination station or in the polyclinic if wounded with objects soiled with saliva or brain matter of animals, or when the saliva of animals gets on the skin or mucous membranes, because only a medical specialist, can decide whether or not in the given case, the vaccine should be given.

Inoculation against influenza. Influenza is the most common infectious disease. There is probably not one single man that has not been sick with it at least once during his life. The harm to the state from loss of working days because of influenza is very great. V.M. Zhdanov cites an interesting calculation that shows that if it were possible to decrease the average loss of work due to influenza only by one day, it would save the government at least 500 million rubles a year.

The search for an effective vaccine against influenza has long been going on in our country and abroad. Scientists in the USA and England have concentrated their attention mainly on killed vaccine used subcutaneously. Although these vaccines do lower the morbidity among the immunized two or three times, they nevertheless have several drawbacks. It

has been proved that killed vaccines are less effective than live ones introduced into the nasal cavity. Moreover, the subcutaneously injected, killed vaccines proved to be much more expensive than the live ones. Finally, it is much more difficult to give a vaccine subcutaneously on a mass scale than to introduce it through the nasal cavity. At the same time, it is absolutely clear that a vaccine against influenza will make sense only when it can be administered to millions of people.

Therefore, the efforts of Soviet scientists to find a live vaccine to be introduced through the nasal cavity prove to be more purposeful. Such a vaccine was prepared in the USSR by A.A. Smorodintsev, V.M. Zhdanov, V.D. Solovyev and M.N. Sokolov. Recently they succeeded in perfecting the manufacturing of this vaccine and in obtaining a vaccine that can be preserved for a long time. Numerous tests have shown that the vaccine against influenza obtained by the Soviet scientists is sufficiently effective. Immunizations with this vaccine reduce the morbidity among the vaccinated no less than three times. Vaccinations into the nasal cavity are absolutely safe and do not cause any reaction. The technical simplicity of the method makes possible its utilization on a wide scale.

The causative agent of influenza is one of the simplest of the known microorganisms, the so-called filterable viruses. There are four known types of the influenza virus. They are A, A1, A2 and B. A person that had influenza caused by one type of virus acquires immunity only against it and can easily become infected with a virus of another type. To create immunity to viruses of the type A, A1, A2, and B, the vaccine, from the very first is prepared from all four types of the causative agents. It is put on the market in a dry form (as a powder). The vaccine can be introduced into the nose as a powder by inhaling it from a spoon and also by means of a special blower. Another method is to dissolve the vaccine in distilled water and put it into the nasal cavity with a dropper. Due to the fact that outbreaks of influenza most frequently appear during the winter and spring season, inoculations against this disease are done in October and November to give the population protection from one to two months before the possible increase in morbidity. The immunization is not given persons suffering with an acute inflammation of the upper respiratory tract or of the throat or patients with active tuberculosis, severe forms of diseases of the kidney, liver and the cardiovascular system. Vaccinations against influenza should not be administered during the second half of pregnancy.



Simultaneously with the influenza vaccine that imparts an active immunity against the disease, passive immunity against influenza is established in persons who had been in contact with the flu patients by introducing ready-made antibodies into the nasal cavity. Anti-influenza serum is used for this purpose. This drug was obtained by A.A. Smorodintsev back in the 30's. At the present time, in order to prevent infection in persons who have come in contact with flu patients, it is recommended to use A.A. Smorodintsev's combined preparation containing the anti-influenza serum, penicillin and norsulfazol. The use of this preparation at the beginning of the outbreak of the disease helps check the outbreak. The influenza vaccine as well as the anti-influenza serum should be given members of large, organized communities: factory workers, students of higher and secondary schools, students F.Z.O. Schools, Factory and Plant Schools medical personnel, etc.

In describing influenza vaccine it is impossible to pass over the last pandemic (international epidemic) of this disease which spread throughout the world in 1957. This pandemic began in Southeastern Asia (Singapore, Malaya, the Philippines) in February and spread rapidly to the West where during the spring and summer season it involved the countries of the Near East, Europe, America and even Australia. The pandemic came to our country in two waves: during the spring and summer in relatively small outbreaks and in autumn with a considerably greater morbidity. It is estimated that on the average up to 40 percent of the earth's population had influenza. It became clear that the pandemic of influenza in 1957 was caused by a new, previously unknown, type of virus. This causative agent appeared as a result of the mutations of viruses in group A and received the name A2 or asiatic virus. It is clear that the population that had been immunized against influenza by the old types of viruses or by vaccines containing the previous types of viruses did not have any immunity against the new virus type A2. As a result of the absence of immunity the population proved to be very susceptible to this virus, which would explain the high rate of infection, and the rapid spread of influenza.

For effective protection against influenza it was urgently necessary to devise a new vaccine containing virus A2. The Soviet scientists solved this complicated problem very quickly. Within two or three months after the first outbreaks of influenza in the USSR they prepared vaccines containing the new virus and giving effective protection against asiatic influenza. At the present time, all the health centers of our country have this vaccine in the quantities needed.



Inoculation against typhus. These vaccinations were developed relatively recently. Initially the typhus vaccine was prepared from the intestines of lice artificially infected with special microbes, rickettsiae, that are the causative agents of typhus. The preparation of this vaccine was labor and time consuming because to grow the rickettsiae it was necessary to infect each individual louse. A.V. Pshenichkov and B.I. Reicher have simplified the method of preparation by finding a way to infect not the mature lice, but their nits. For this purpose, skin taken from a cadaver is stretched over a special vessel. Blood and live rickettsiae are placed in the vessel. The nits adhere to the stretched skin and become infected with rickettsiae. After several days when many rickettsiae have accumulated in the intestine of the nit, they are mashed into pulp and, formalin or carbolic acid are added to kill the rickettsiae. The vaccine is prepared from the killed rickettsiae.

In our country, the vaccine prepared by the method of M.K. Krontovskaya and M.M. Mayevskiy from the lungs of white mice infected with rickettsiae has been widely used. The mice are infected by dropping the infectious material into the nasal cavity. As a result, they develop rickettsial pneumonia during which many rickettsiae accumulate in the pulmonary tissues. The mice are then killed, their lungs ground and converted to a liquid emulsion, after which the rickettsiae are killed by formalin.

The typhus vaccine has an auxiliary function. Owing to the fact that today the disease is rare, mass vaccinations against typhus are not conducted. The vaccine is used mainly to protect persons who run the risk of infection with typhus, such as medical personnel and employees of bath houses, laundries and barber shops.

Inoculation against other infectious diseases. Effective vaccines against several other infectious diseases have been obtained in the USSR. Should the need arise, vaccinations against the Weil-Vasilyev infectious jaundice, caused by a special type of microbe -- the spirochete, are available. Also available are vaccines against epidemic encephalitis transmitted by ticks (tick encephalitis), against pneumonia caused by a special type of rickettsiae, so-called "Q" fever and against several other diseases. However, due to the fact that these diseases rarely occur in the USSR or are seen in limited areas only there is no need to elaborate in detail on these inoculations.

The Soviet scientists continue to work on the improvement and development of even those vaccines which are used against diseases that have been completely eliminated in our country.

An example of work in this direction is the effective, live vaccine against the plague developed by M.P. Pokrovskaya, N.N. Zhukov-Verezhnikov and S.I. Korobkova.

The scientists, however, have not yet been able to obtain effective vaccines against all diseases. For example, we still do not have an available vaccine against epidemic hepatitis (Botkin's disease), against so common an infectious disease of childhood as scarlet fever and against some other infectious diseases.

The persevering work of our native researchers and the broad opportunities afforded by the Soviet government whose main objective always was and will be concern for the prosperity and health of the people, hold the promise of new discoveries of effective vaccines and sera, to protect man from infectious disease.

An illustration of the successful work in the field of disease prevention is the vaccine against the mumps (epidemic parotitis, a common disease of childhood. This vaccine was obtained by the Leningrad scientists A.A. Smorodintsev, N.S. Klyachko and others who were able to develop a quick and simple method of isolating the virus, the causative agent of this disease, from the saliva of sick children and infecting with it growing chicken embryos. As a result of repeated multiple transfers from one chick embryo to another, the virus loses its infective characteristics with regard to man. After 15 transfers it becomes safe and when introduced into the organism of a child (into the oral cavity, intradermally or subcutaneously) does not cause the disease. At the same time this attenuated virus multiplies in the organism and causes the formation of a high immunity against mumps.

Thus the epidemic parotitis vaccine consists of live attenuated viruses. The first tests of the vaccine showed that it was well tolerated and sufficiently effective. Immunity against mumps in the vaccinated develops after two to three weeks following a single subcutaneous or intradermal injection with the vaccine. In 1956 in Leningrad successful inoculations against the mumps were given to more than 25 thousand children under the age of ten. These vaccinations established the high effectiveness of the new vaccine. In particular, it became apparent that the vaccine developed by Soviet scientists is much more effective than the killed vaccine obtained in the US: The domestic vaccine decreases the morbidity with mumps among the inoculated almost ten times, the American killed vaccine -- only two to three times.

The development of a vaccine against epidemic parotitis and its use by the department of health will assure a considerable reduction in the morbidity of this disease among children.

The continuing development of the science of prophylactic inoculations and the discovery of new effective vaccines and sera are the actual prerequisites for a victorious battle with infectious diseases in our country.

END